

NEWS 17 MAY 21 CA/CAplus enhanced with additional kind codes for German patents
NEWS 18 MAY 22 CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS 19 JUN 27 CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS 20 JUN 29 STN Viewer now available
NEWS 21 JUN 29 STN Express, Version 8.2, now available
NEWS 22 JUL 02 LEMBASE coverage updated
NEWS 23 JUL 02 LMEDLINE coverage updated
NEWS 24 JUL 02 SCISEARCH enhanced with complete author names
NEWS 25 JUL 02 CHEMCATS accession numbers revised
NEWS 26 JUL 02 CA/CAplus enhanced with utility model patents from China
NEWS 27 JUL 16 CAplus enhanced with French and German abstracts
NEWS 28 JUL 18 CA/CAplus patent coverage enhanced

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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=> VH and VL and antibody and catalytic (w) antibody

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=> s VH and VL and antibody and catalytic (w) antibody

L1 45 VH AND VL AND ANTIBODY AND CATALYTIC (W) ANTIBODY

=> s l1 and polypeptide

L2 6 L1 AND POLYPEPTIDE

=> d ibib abs 12 1-6

L2 ANSWER 1 OF 6 MEDLINE on STN

ACCESSION NUMBER: 96279092 MEDLINE

DOCUMENT NUMBER: PubMed ID: 8663068

TITLE: Selection of linkers for a catalytic single-chain antibody using phage display technology.

AUTHOR: Tang Y; Jiang N; Parakh C; Hilvert D

CORPORATE SOURCE: Departments of Chemistry and Molecular Biology, The Scripps Research Institute, La Jolla, California 92037, USA.

SOURCE: The Journal of biological chemistry, (1996 Jun 28) Vol. 271, No. 26, pp. 15682-6.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199608

ENTRY DATE: Entered STN: 28 Aug 1996

Last Updated on STN: 3 Feb 1997

Entered Medline: 20 Aug 1996

AB Phage display has been evaluated as a means of rapidly selecting tailored linkers for single-chain antibodies (scFvs) from protein linker libraries. Preliminary experiments with a conventional linker failed to yield a functional single-chain version of a catalytic antibody with chorismate mutase activity. A random linker library was therefore constructed in which the genes for the heavy and light chain variable domains were linked by a segment encoding an 18-amino acid polypeptide of variable composition. The scFv repertoire (approximately 5 x 10(6) different members) was displayed on filamentous phage and subjected to affinity selection with hapten. The population of selected variants exhibited significant increases in binding activity but retained considerable sequence diversity. Screening 1054 individual variants subsequently yielded a catalytically active scFv that was produced efficiently in soluble form. Sequence analysis revealed a conserved proline in the linker two residues after the VH C terminus and an abundance of arginines and prolines at other positions as the only common features of the selected tethers. There are apparently many viable solutions to the problem of linking individual VH and VL domains, but subtle differences in sequence dramatically influence the production, stability, and recognition properties of the scFv. The success of these experiments suggests that phage display will be generally useful for identifying peptide sequences for covalently linking any two protein domains.

L2 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:438341 BIOSIS
DOCUMENT NUMBER: PREV200300438341
TITLE: Changes in structure and dynamics of the Fv fragment of a catalytic antibody upon binding of inhibitor.
AUTHOR(S): Kroon, Gerard J. A.; Mo, Huaping; Martinez-Yamout, Maria A.; Dyson, H. Jane [Reprint Author]; Wright, Peter E. [Reprint Author]
CORPORATE SOURCE: Department of Molecular Biology, Scripps Research Institute, 10550 N. Torrey Pines Road, MB2, La Jolla, CA, 92037, USA
dyson@scripps.edu; wright@scripps.edu
SOURCE: Protein Science, (July 2003) Vol. 12, No. 7, pp. 1386-1394. print.
ISSN: 0961-8368.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Sep 2003
Last Updated on STN: 24 Sep 2003

AB Binding of the product inhibitor p-nitrophenol to the monoclonal esterolytic antibody NPN43C9 has been investigated by performing NMR spectroscopy of the heterodimeric variable-domain fragment (Fv) of the antibody in the presence and absence of inhibitor. Structural information from changes in chemical shift upon binding has been related to the changes in local dynamics in the active site of the catalytic antibody using NMR relaxation measurements. Significant changes in the chemical shifts of the backbone resonances upon binding extend beyond the immediate vicinity of the antigen binding site into the interface between the two associated polypeptides that form the Fv heterodimer, a possible indication that the binding of ligand causes a change in the relative orientations of the component light (VL) and heavy (VH) chain polypeptides. Significant differences in backbone dynamics were observed between the free Fv and the complex with p-nitrophenol. A number of resonances, including almost all of the third hypervariable loop of the light chain (L3), were greatly broadened in the free form of the protein. Other residues in the antigen-binding site showed less broadening of resonances, but still required exchange terms (Rex) in the model-free dynamics analysis, consistent with motion on a slow timescale in the active site region of the free Fv. Binding of p-nitrophenol caused these resonances to sharpen, but some Rex terms are still required in the analysis of the backbone dynamics. We conclude that the slow timescale motions in the antigen-binding site are very different in the bound and free forms of the Fv, presumably due to the damping of large-amplitude motions by the bound inhibitor.

L2 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:857619 CAPLUS
DOCUMENT NUMBER: 141:348835
TITLE: Production of antibodies with covalently reactive antigen analogues for treating autoimmune disease, cancer, infection and Alzheimer's disease.
INVENTOR(S): Paul, Sudhir; Nishiyama, Yasuhiro
PATENT ASSIGNEE(S): The University of Texas, USA
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

WO 2004087735 A2 20041014 WO 2004-US9398 20040326
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
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TD, TG

CA 2520381 A1 20041014 CA 2004-2520381 20040326
EP 1615946 A2 20060118 EP 2004-758448 20040326

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

US 2007105092 A1 20070510 US 2006-581294 20060601

PRIORITY APPLN. INFO.: US 2003-458063P P 20030326
US 2004-534689P P 20040108
WO 2004-US9398 W 20040326

AB Improved methods for the production, selection and inhibition of proteolytic or catalytic and covalent antibodies are disclosed. The methods use covalently reactive polypeptide antigen analogs (pCRAs) and water-binding pCRAs (pCRAws) to stimulate the production of antibodies. The invention also provides methods for screening antibodies from phage display antibody libraries. The antibodies may be monoclonal antibodies, polyclonal antibodies, antibody fragments, IgG, IgM, IgA, IgD, IgE, VH or VL. These antibodies are specific to pCRAs containing gp120, VIP, factor VIII, EGF receptor, CD4, β -amyloid peptide 1-40 or 1-42, etc., and are passive immunotherapy of infection, blood coagulation disorder, cancer, autoimmune disease, alloimmune disease, lymphoproliferative disease, hepatitis C, Alzheimer's disease, etc.

L2 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:513781 CAPLUS

DOCUMENT NUMBER: 140:14270

TITLE: Changes in structure and dynamics of the Fv fragment of a catalytic antibody upon binding of inhibitor

AUTHOR(S): Kroon, Gerard J. A.; Mo, Huaping; Martinez-Yamout, Maria A.; Dyson, H. Jane; Wright, Peter E.

CORPORATE SOURCE: Department of Molecular Biology and Skaggs Institute of Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Protein Science (2003), 12(7), 1386-1394

CODEN: PRCIEI; ISSN: 0961-8368

PUBLISHER: Cold Spring Harbor Laboratory Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Binding of the product inhibitor p-nitrophenol to the monoclonal esterolytic antibody NPN43C9 has been investigated by performing NMR spectroscopy of the heterodimeric variable-domain fragment (Fv) of the antibody in the presence and absence of inhibitor. Structural information from changes in chemical shift upon binding has been related to the changes in local dynamics in the active site of the catalytic antibody using NMR relaxation measurements. Significant changes in the chemical shifts of the backbone resonances upon binding extend beyond the immediate vicinity of the antigen binding site into the interface between the two associated polypeptides that form the Fv heterodimer, a possible indication that the binding of ligand causes a change in the relative orientations of the component light (VL) and heavy (VH) chain polypeptides. Significant differences in backbone dynamics were observed between the free Fv and the

complex with p-nitrophenol. A number of resonances, including almost all of the third hypervariable loop of the light chain (L3), were greatly broadened in the free form of the protein. Other residues in the antigen-binding site showed less broadening of resonances, but still required exchange terms (Rex) in the model-free dynamics anal., consistent with motion on a slow timescale in the active site region of the free Fv. Binding of p-nitrophenol caused these resonances to sharpen, but some Rex terms are still required in the anal. of the backbone dynamics. We conclude that the slow timescale motions in the antigen-binding site are very different in the bound and free forms of the Fv, presumably due to the damping of large-amplitude motions by the bound inhibitor.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:594353 CAPLUS
DOCUMENT NUMBER: 127:289747
TITLE: Cleavage specificity of a proteolytic antibody light chain and effects of the heavy chain variable domain
AUTHOR(S): Sun, Mei; Gao, Qing-Sheng; Kirnarskiy, Leonid; Rees, Anthony; Paul, Sudhir
CORPORATE SOURCE: Department of Anesthesiology and Eppley Cancer Research Institute, University of Nebraska Medical Center, Omaha, NE, 68198-6830, USA
SOURCE: Journal of Molecular Biology (1997), 271(3), 374-385
CODEN: JMOBAK; ISSN: 0022-2836
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The recombinant light chain (L chain) of an antibody raised by immunization with vasoactive intestinal polypeptide (VIP) cleaved this peptide on the C-terminal side of basic residues. The major sites of cleavage in VIP were two adjacent peptide bonds, Lys20-Lys21 and Lys21-Tyr22. Lower levels of cleavage were evident at Arg14-Lys15 and Lys15-Gln16. Hydrolysis of radiolabeled VIP by the L chain was inhibited by two serine protease inhibitors, diisopropylfluorophosphate and aprotinin, but not by soybean or lima bean trypsin inhibitors or inhibitors of other classes of proteases. To probe the role of the VH domain, single chain Fv constructs composed of the VL domain of the anti-VIP L chain linked via a 14-residue peptide to its natural VH domain partner or an irrelevant anti-lysozyme VH domain (hybrid FV) were prepared. The anti-VIP FV hydrolyzed VIP with K_s 21.4-fold lower than the L chain and 250-fold lower than the hybrid FV, suggesting increased affinity for the substrate ground state due to the anti-VIP VH domain. The kinetic efficiency (k_{cat}/K_s) of the anti-VIP FV was 6.6-fold greater compared to the L chain and 29.4-fold greater compared to the hybrid Fv. Peptide-MCA substrates unrelated in sequence to VIP were hydrolyzed by the anti-VIP Fv and L chain at equivalent rates. These observations lead to a model of catalysis by the anti-VIP Fv in which the essential catalytic residues are located in the VL domain and addnl. residues from the VH domain are involved in high affinity binding of the substrate.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:391215 CAPLUS
DOCUMENT NUMBER: 125:80129
TITLE: Selection of linkers for a catalytic single-chain antibody using phage display technology
AUTHOR(S): Tang, Ying; Jiang, Ning; Parakh, Cushrow; Hilvert, Donald
CORPORATE SOURCE: Dep. Chem. Mol. Biol., Scripps Res. Inst., La Jolla,

SOURCE: CA, 92037, USA
Journal of Biological Chemistry (1996), 271(26),
15682-15686

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Phage display has been evaluated as a means of rapidly selecting tailored linkers for single-chain antibodies (scFvs) from protein linker libraries. Preliminary expts. with a conventional linker failed to yield a functional single-chain version of a catalytic antibody with chorismate mutase activity. A random linker library was therefore constructed in which the genes for the heavy and light chain variable domains were linked by a segment encoding an 18-amino acid polypeptide of variable composition. The scFv repertoire ($\approx 5 \times 10^6$ different members) was displayed on filamentous phage and subjected to affinity selection with hapten. The population of selected variants exhibited significant increases in binding activity but retained considerable sequence diversity. Screening 1054 individual variants subsequently yielded a catalytically active scFv that was produced efficiently in soluble form. Sequence anal. revealed a conserved proline in the linker two residues after the VH C terminus and an abundance of arginines and prolines at other positions as the only common features of the selected tethers. There are apparently many viable solns. to the problem of linking individual VH and VL domains, but subtle differences in sequence dramatically influence the production, stability, and recognition properties of the scFv. The success of these expts. suggests that phage display will be generally useful for identifying peptide sequences for covalently linking any two protein domains.

EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|------|-------------------------------------|--------------------------------|------------------|---------|------------------|
| L1 | 0 | VH adj antibody and VL adj antivodt | US-PGPUB; USPAT; DERWENT | OR | ON | 2007/07/25 09:49 |
| L2 | 64 | VH adj antibody and VL adj antibody | US-PGPUB; USPAT; DERWENT | OR | ON | 2007/07/25 09:50 |
| L3 | 4 | I2 and catalytic adj antibody | US-PGPUB; USPAT; DERWENT | OR | ON | 2007/07/25 09:50 |